

Cannabis and Psychosis

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Drug use and Psychotic Disorders

About 50% of individuals with schizophrenia or other psychotic disorders abuse drugs, typically *cannabis*, *tobacco* and *alcohol*.

This comorbidity is higher than what would be expected if psychosis and drug use were independent.

This comorbidity is prevalent in first-episode psychosis patients, including adolescents (also with cannabis the most commonly used drug).

The use of cannabis in particular is associated with psychosis severity in cross-sectional studies.

Cannabis and Psychosis in a Developmental Context

Adolescence is a critical period characterized by profound changes in the brain and in behavior.

Normal changes lead to age-specific behaviors such as peer affiliation and experimentation with drugs.

Changes occur in the reward system (dopamine) such that drugs and risk-taking are more rewarding for adolescents.

Receptors for cannabis in the brain peak during adolescence – these are densely interconnected with the dopamine system in the striatum, which has been implicated in psychotic disorders.

Trajectory to Schizophrenia

Toddlers: developmental delays



4–6 years: isolated play and speech problems

7 and 11 years: some clumsiness

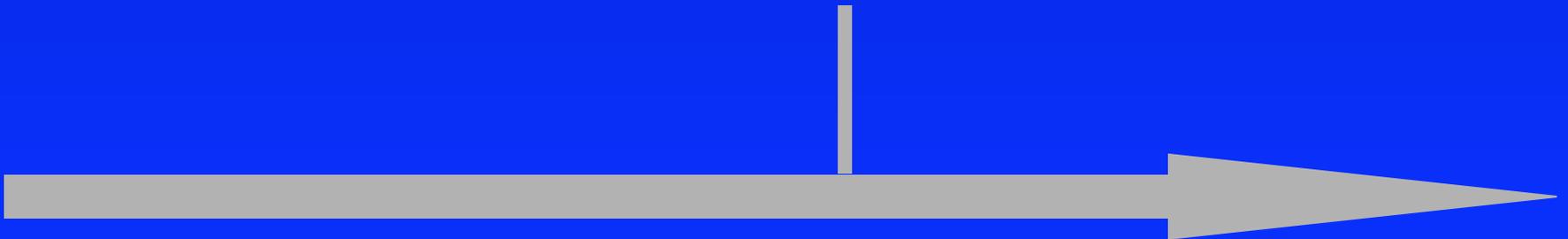
Teen years: poor school performance, social anxiety



Initiation of Drug Use



Teen years: liability to drug use

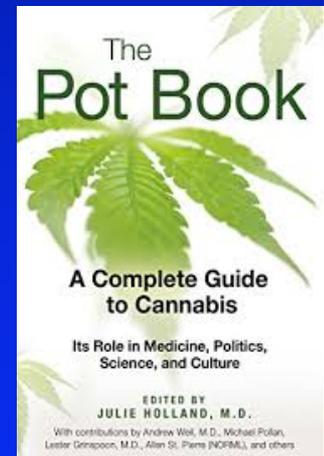


The Debate

UK: A decade ago, the Lancet published a systematic review (Moore, 2007), which concluded that “the evidence is consistent with the view that cannabis increases risk of psychotic outcomes”.

Critics and naysayers: A new “reefer madness”? Is this true? Or could it just be that young people developing psychosis are more prone to using drugs such as cannabis? (Confounds)

In support: observed association, temporal sequence, dose-dependency, biological plausibility, specificity. See my chapter in the POT BOOK!



History: cannabis leads to paranoia

19th century France: the Club de Haschischins, frequented by Victor Hugo, Dumas, Baudelaire, and Delacroix

The French psychiatrist, Moreau de Tours, took large doses of cannabis at the Club de Haschischins, giving cannabis also to students and patients.

They were noted to become paranoid.



Self-report of psychotogenic properties

A random sample of individuals ages 18-35 in New Zealand showed that 14% of cannabis users reported “strange, unpleasant experiences such as hearing voices or becoming convinced that someone is trying to harm them” after smoking cannabis (Thomas, 1996).

Such transient psychotic symptoms may not be benign, especially in young people, in whom they are associated with risk for later psychotic disorder (Arseneault, 2004; Henquet, 2005).

Daily Diary Studies – Experience Sampling

In Bordeaux (Verdoux et al., 2003), college students kept track of their drug use and any psychotic symptoms

Those with “psychosis proneness” developed “unusual perceptions and feelings of thought influence” after smoking cannabis.

They also became more anxious (other students felt calmer).

The use of amphetamines did not explain these apparent effects.

Of note, cannabis use didn't follow the psychotic-like symptoms (i.e. not “self-medication”).

What about *earlier* cannabis use as a risk factor for psychotic disorder? Epidemiological studies

Sweden (Andreasson, 1987; Zammit, 2002).

~ 45,000 young men drafted into the army (healthy)

Cannabis users were twice as likely to develop schizophrenia within 15 years

Heavy users (>50 occasions) were six times as likely to develop schizophrenia within 15 years

Not accounted for by low IQ, poor social function or the use of tobacco, alcohol or other drugs

Not accounted for by “prodromal” symptoms

And . . . Dunedin study (NZ) – Arseneault, 2002

1000 children, assessed at :

Age 11 - any psychotic-like symptoms

Ages 15 and 18 – any cannabis use

Age 26 – development of schizophreniform disorder

Cannabis use at age 18: 50% increase in schizophrenia BUT

Cannabis use at age 15: 300-400% increase in schizophrenia

i.e. 10% of those individuals who had used cannabis by age 15 developed schizophreniform disorder!

Not accounted for by psychotic-like symptoms at age 11.

The use of *other* drugs did not increase risk for schizophrenia.

Cannabis use did not increase the risk for later depression.

Interaction with genetic variation at the COMT gene

Naysayers:

If cannabis use can lead to psychosis, why isn't there an epidemic of schizophrenia?

- 1) There may already be an “epidemic” in some areas where potent cannabis is widely used – the Gambia (Rolfe, 1993) and inner-city London (Boydell, 2006). Di Forti (2019) showed high-potency cannabis accounted for differences in psychosis incidence among European countries (OR 3.2 for daily use vs. never use)
- 2) Cannabis use may simply advance the onset of psychosis in those destined to become psychotic eventually (e.g. di Forti, 2014). (Not trivial if this can be forestalled)
- 3) As mentioned, only a subset of the population may be vulnerable to developing psychosis in response to cannabis use. Most people are likely not.

Criteria for the Psychosis Prodrome

- Help-seeking adolescents and young adults with
 - Subthreshold psychotic symptoms (illusions, overvalued ideas, and suspiciousness instead of hallucinations, delusions, and paranoia) *and/or*
 - A first-degree relative with psychosis *plus* a decline in function over 1 year *and/or*
 - Brief, intermittent psychotic symptoms (<1 week)
- *CHR patients have ~ 25% risk of a psychosis onset in 1–2 years*

Clinical High Risk studies: Cannabis and Psychotic-like symptoms over time

We found half of the young people in our CHR program used drugs, in particular cannabis (less so cocaine, amphetamine and hallucinogens). *Corcoran. . Malaspina, 2008.*



When these at-risk youths were followed, psychotic-like symptoms (perceptual disturbances) and anxiety fluctuated over time with cannabis use.

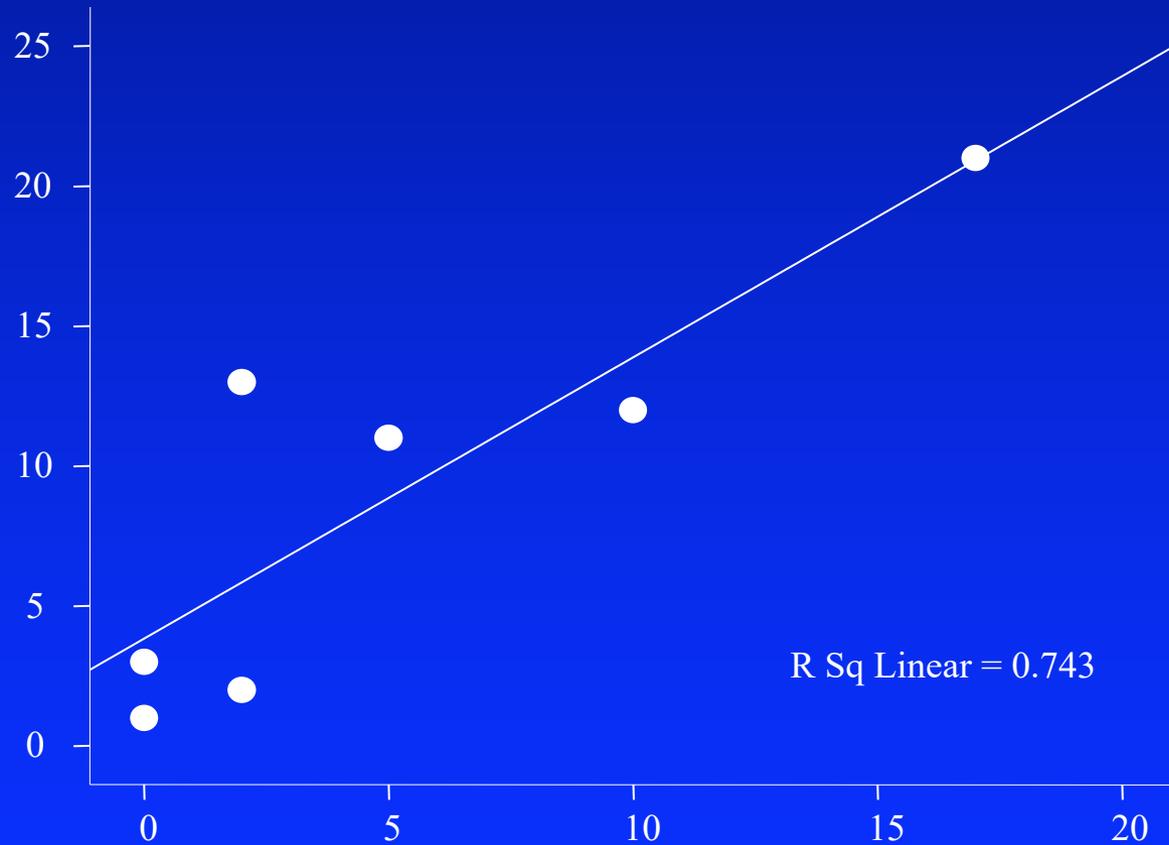
NB – no incident drug use in non-users.

Qualitative data– Participants said they smoked when they felt better, with psychotic-like symptoms following over the next few days.



ONE PATIENT

Psychotic-like symptoms



Reported number of days of cannabis use in the previous month

<http://www.shroomery.org/forums>: Reviews of my paper 😊

I am unable to comment on the statistical methods because I have not read the study.

I think it is safe to say that no matter what methods they used, a study of this type with only 32 people (just 13 cannabis users) could not possibly produce meaningful results.

Its probably not possible to get useful results even with a very large study because people with mental problems often medicate with cannabis.

I can't think of any way to separate correlation from causation, but fortunately for the authors of the study they don't need to since they can just spew propaganda instead.

<http://www.shroomery.org/forums>

i dont even believe that.

we have been seeing this kind of junk science for years.

and what seuss said below is correct.

the sample size, way too small

obviously too many variables.

and i dont think this so called study is even new
anyway.

Reviews of my paper continued 😊

Re: Cannabis use linked to early psychosis symptoms in susceptible people

[Re: [b0red5tiff](#)]

[#8990397](#) - 09/26/08 04:58 PM

Quote:

To investigate, the researchers studied 32 patients, aged 25 years or younger, who showed early signs of developing psychosis.

Wow what a large sample size! Top notch science work here.

Quote:

But the team also found that cannabis users experienced more early psychosis symptoms, such as perceptual disturbances, and worse functioning during episodes of increased cannabis use than at other times, and compared with other participants.

Umm maybe they were stoned? NEWS FLASH: Weed gets you stoned.

So, if I understand correctly, the point of the article is that marijuana use brings about mental illnesses in people predisposed for mental illness? How is this idea new?

Reasons for Cannabis Use in CHR Youths (Gill, 2017)

Corcoran, 2008. Qualitative – Participants said they smoked when they felt better, with psychotic-like symptoms over the next few days, so we did a survey (Spencer 2012 Reasons for Use)



Enhancement

Because it makes you feel good

Because it's fun

To get high

Social Motive

Because it's what most of your friends do when you get together

Because it makes social gatherings more enjoyable

As a way to celebrate

To be sociable

Coping with Unpleasant Affect

To relax

Because it helps when you are feeling nervous

Because it helps when you are feeling depressed

To forget your worries

To feel motivated

To make it easier to sleep

To help me concentrate

As in schizophrenia, and in adolescents with other psychiatric issues . . .

CHR youths reported using MJ primarily for mood enhancement.

This was especially true in those with trait anhedonia.

Social anxiety was associated with social motives, desire for acceptance and coping with unpleasant affect.

But can cannabis use lead to psychotic *disorder* in at-risk youths?

Clinical high risk samples:



Does baseline cannabis use predict conversion to psychosis?

No. Seven negative studies (including our own N = 200)

But Kraan, 2016, in a meta-analysis found cannabis *abuse and dependence* is predictive of psychosis onset in CHR, even if cannabis use per se is not.

Effects of cannabis in vivo: Modern *challenge* studies

At Yale, D'Souza and colleagues gave an active ingredient of cannabis, delta-9-THC in *intravenous* form to normal individuals and patients with schizophrenia.

This led to anxiety, cognitive deficits and psychotic symptoms.

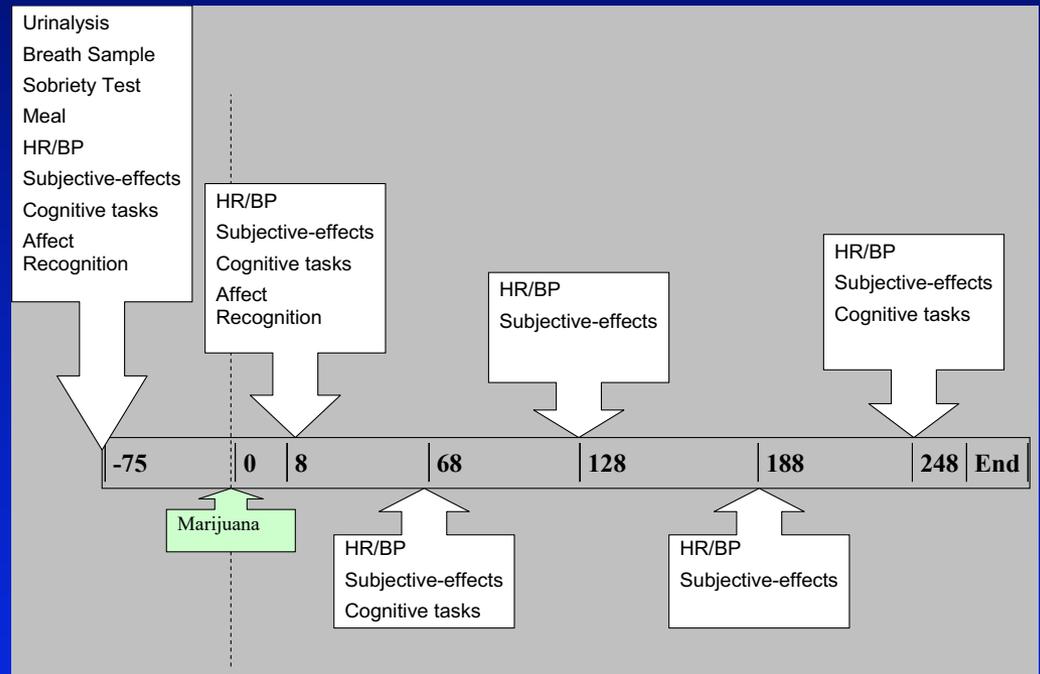
However, *smoking marijuana* doesn't seem to lead in the short term to psychotic symptoms in most people, but does in individuals with psychosis.

And also seems to in individuals at clinical high risk for psychosis

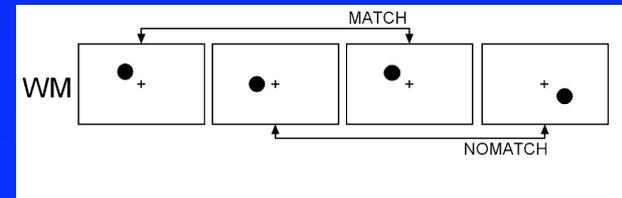
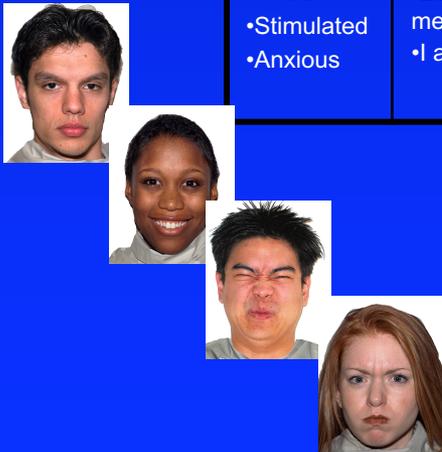
Acute effects of smoked MJ in MJ smokers at CHR

Vadhan et al., 2017

Thurs	Task training
Mon, Thurs, Mon	0.0%, 5.5%, 1.8% (counterbalanced Δ^9 THC)

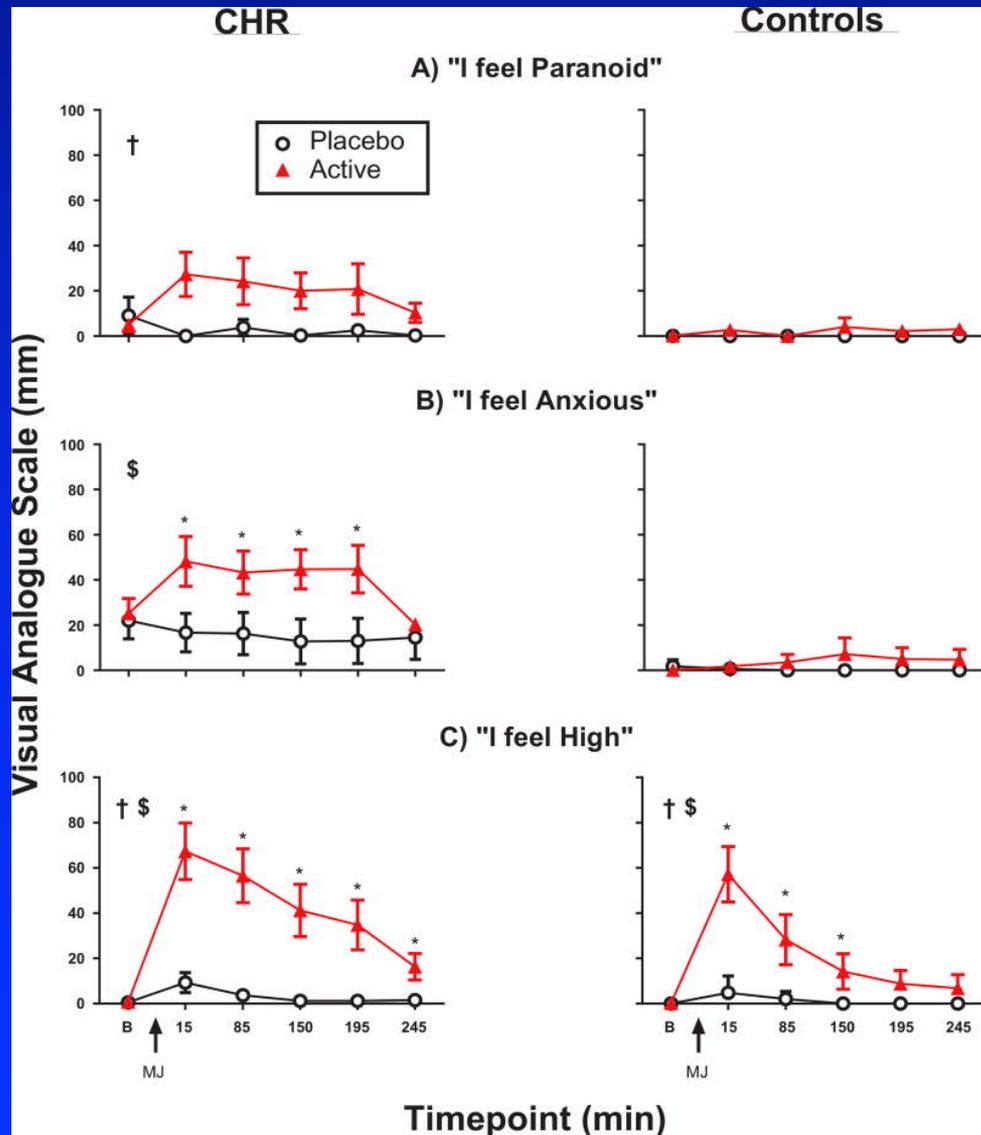


Mood	Paranoia/persecution	Thought control	Grandiosity/religious	Perceptual
<ul style="list-style-type: none"> •High •Good •Stimulated •Anxious 	<ul style="list-style-type: none"> •I can trust other people •Like people are out to get me •I am being watched 	<ul style="list-style-type: none"> •I can read others' minds •others can hear my thoughts •somebody else controls my thoughts 	<ul style="list-style-type: none"> •I can predict the future •I have special powers or abilities •I am famous •I have been chosen by God for a higher purpose 	<ul style="list-style-type: none"> •I hear sounds or voices others can't •I see things others can't •I feel tingling in my skin

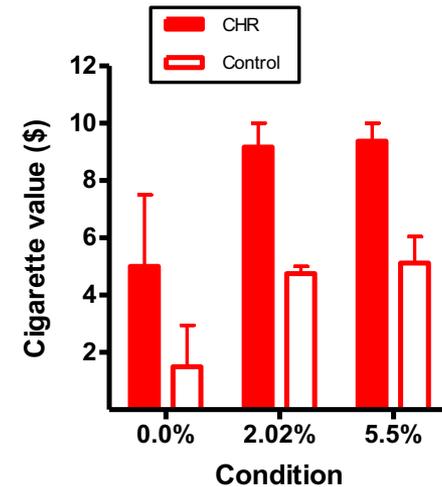


Spatial *n*-Back (Ilan et al., 2003)

CHR report more paranoia and anxiety when they smoke MJ, but also a greater high (Vadhan 2017)



Also, slowed time perception, visual illusions, feelings of strangeness, decreased working memory performance, and increased valuation of MJ cigarette.



No increase in hallucinations, depression, or loneliness. No effect on attention or reaction time. Similar increase in arousal (heart rate).

Implications of CB use in FEP

FEP – 35 to 45% use cannabis.

Cannabis use predicts

- low medication adherence and less remission (Colizzi 2016)
- increased risk of relapse (Schoeler 2016)
- more legal involvement (Rolin et al., 2018)
- less weight gain (!), more normal triglycerides, LDL and fasting blood sugar (Schleffer 2018; replicated by Vasquez-Bourgon 2019)

To the Editor:

The pro-legalization side has intentionally obscured the dangers of marijuana, as Alex Berenson points out. The tragedy is that if we discussed those dangers openly, we could address them.

Marijuana legalization will harm our children. Mitigating these harms does not require putting people in prison; what we need are thoughtful, well-resourced public health strategies.

Our experiences with tobacco, alcohol, vaping and even opioids have taught us what works, and what mistakes we should not repeat. Taxes on marijuana will not pay for the health consequences and treatment for people who become addicted. The marijuana industry should not be allowed to regulate itself and must be prohibited from advertising to kids. A legal purchase age of 21 will not keep marijuana out of children's hands. We must invest heavily in prevention programs.

Sadly, states that have legalized recreational marijuana have ignored the dangers to kids and the lessons of the past, and have charged ahead as if marijuana were harmless.

Emily Feinstein
New York

The writer is executive vice president of the Center on Addiction.

Potential interventions – behavioral?

Psychological treatments for cannabis use in FEP

Edwards 2006 – MI plus CBT – no effect

Bonsack 2011 – MI – short-term reduction in CB use

Hjorthøj 2012 – MI plus CBT – no effect

Madigan 2013 – MI plus CBT – no effect

All only 3-6 months long – need longer trial of MI plus CBT?

Barrowclough 2014: N = 110; Standard care vs. standard care plus MI/CBT (short -12 sessions in 4.5 mos OR long - 24 sessions in 9 mos)

No reduction in frequency or amount of CB use. No effect on symptoms, function, hospital admissions or relapse.

Planned (Johnson 2016):

CIRCLE – contingency management (financial rewards to effect behavioral change). Psychoeducation +/- payment for clean urine

Potential interventions – medications?

No medications have been found to be effective in reducing cannabis use in adolescents in general OR in young adults with psychotic disorder.

Nielsen 2019 – Cochrane report on pharmacotherapies for CB dependence

Nope! – SSRIs, mood stabilizers, buspirone

GABA pentin? Oxytocin? Atomoxetine?Insufficient evidence

Cannabidiol?

Hahn et al., 2018 – CBD is anxiolytic, antipsychotic and neuroprotective (may also counter negative effects of delta 9 THC) – theoretically should work

McGuire – CBD reduces severity of prodromal symptoms

Neurostimulation? (TMS worked in one study)

Overall

It has been estimated that cannabis use can account for 8-13% of all cases of schizophrenia, which is higher than that associated with having a 1st degree family member with psychosis.

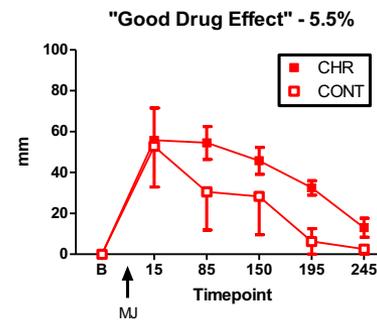
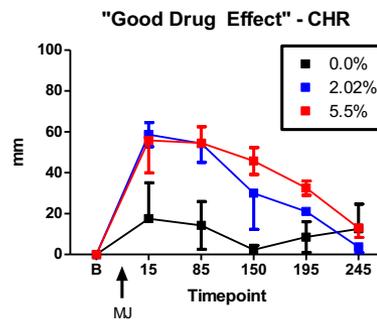
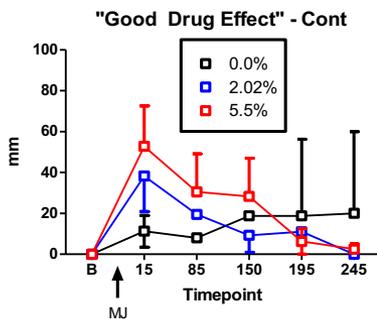
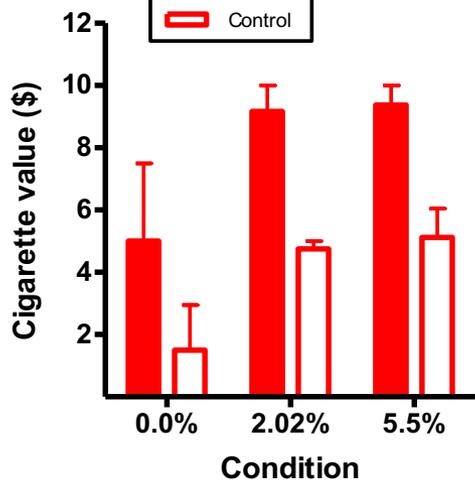
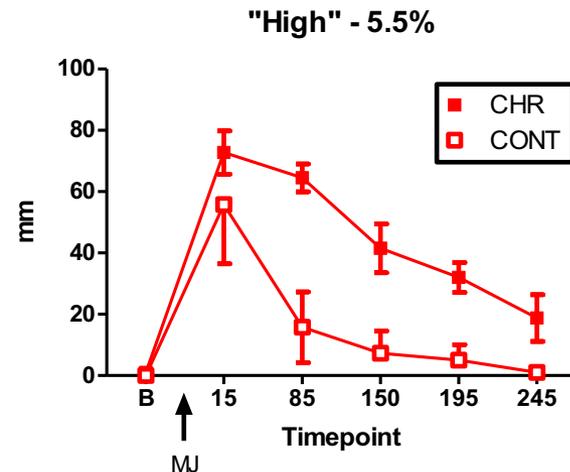
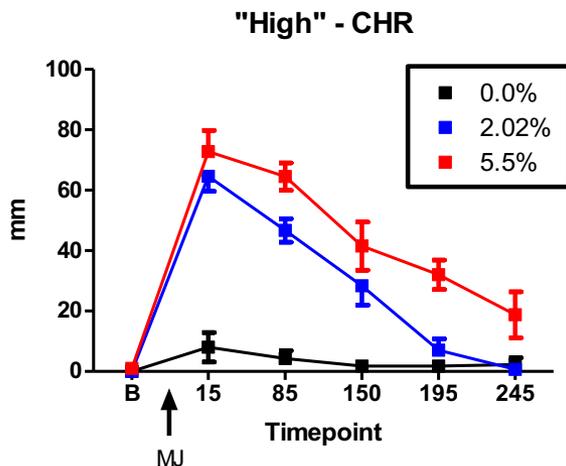
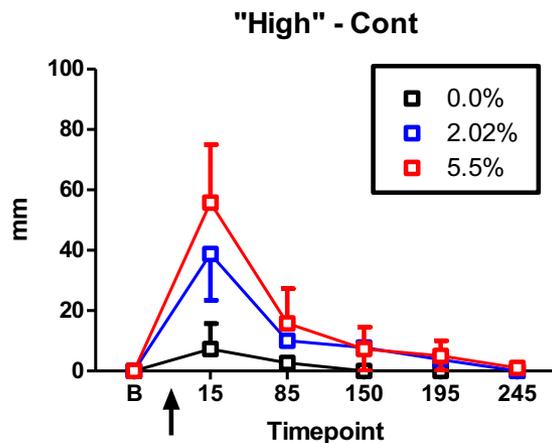
AND cannabis use can be modified, unlike genes.

Even if cannabis use does not cause psychosis, it can worsen outcome for individuals who do become psychotic.

We need effective interventions to reduce cannabis use in individuals with psychosis risk or recent-onset psychosis.

What ideas do you have? What have you found to be effective for addressing cannabis use ?

Intoxication and Rewarding Effects – CHR youths report greater “high” from MJ



But induced paranoia and anxiety are also higher

